Claims:

1. An isolated nucleic acid sequence encoding a polypeptide having transcriptional activation activity, selected from the group consisting of:

(a) a nucleic acid sequence having at least 70% identity with the nucleic acid sequence of SEQ ID NO: 1 or SEQ ID NO: 48;

(b) a nucleic acid sequence encoding a polypeptide having an amino acid sequence which has at least 50% identity with the amino acid sequence of SEQ ID NO: 2 or SEQ ID NO: 49;

(c) a nucleic acid sequence which hybridizes under low stringency conditions with (i) the nucleic acid sequence of SEQ ID NO: 1 or SEQ ID NO: 48, or (ii) its complementary strand, wherein the low stringency conditions are defined by prehybridization and hybridization at 42°C in 5x SSPE, 0.3% SDS, 200 micro g/ml sheared and denatured salmon sperm DNA, and 25% formamide, and wash conditions are defined by 50°C for 30 minutes in 2X SSC, 0.2% SDS;

(d) an allelic variant of (a), (b), or (c);

(e) a subsequence of (a), (b), (c), or (d), wherein the subsequence encodes a polypeptide fragment which has transcriptional activation activity; and

(f) a subsequence of (a), (b), (c), or (d), wherein the subsequence encodes a polypeptide with the amino acid sequence of SEQ ID NO: 3.

2. The nucleic acid sequence of claim 1 which has at least 70%, preferably at least 80%, more preferably at least 85%, even more preferably at least 90%, most preferably at least 95%, even most preferably at least 97%, and even more preferred at least 99% identity with the nucleic acid sequence of SEQ ID NO: 1 or SEQ ID NO: 48.

3. The nucleic acid sequence of claim 1 which has the nucleic acid sequence of SEQ ID NO: 1 or SEQ ID NO: 48.

4. The nucleic acid sequence of any of claims 1 to 3 which encodes a polypeptide comprising an amino acid sequence which has at least 50%,

preferably at least 60%, preferably at least 70%, more preferably at least 80%, even more preferably at least 90%, and most preferably at least 95% identity with the amino acid sequence of SEQ ID NO: 2 or SEQ ID NO: 49.

5. The nucleic acid sequence of any of claims 1 to 4, wherein the nucleic acid sequence is obtained from a fungal cell or a yeast cell.

6. The nucleic acid sequence of claim 5, wherein the fungal cell is a filamentous fungal cell.

7. The nucleic acid sequence of claim 6, wherein the filamentous fungal cell is an *Aspergillus*, *Fusarium*, *Penicillium*, or *Trichoderma* cell.

8. The nucleic acid sequence of claim 7, wherein the *Aspergillus* cell is a strain of *Aspergillus niger* or *Aspergillus oryzae*, or a respective synonym or teleomorph thereof.

9. The nucleic acid sequence of claim 8, wherein the *Aspergillus* cell is a strain of *Aspergillus niger* DSM 12298 or *Aspergillus oryzae* IFO4177.

10. The nucleic acid sequence of claim 7, wherein the *Fusarium* cell is a strain of *Fusarium venenatum*, or a synonym or teleomorph thereof.

11. The nucleic acid sequence of claim 5, wherein the yeast cell is a *Hansenula*, *Pichia*, or *Saccharomyces* cell.

12. The nucleic acid sequence of any of claims 1 to 11 which encodes a polypeptide comprising the amino acid sequence of SEQ ID NO: 2 or SEQ ID NO: 49, or a fragment thereof, which has transcriptional activation activity.

13. The nucleic acid sequence of any of claims 1 to 11 which encodes a polypeptide comprising the amino acid sequence of SEQ ID NO: 3.

14. The nucleic acid sequence of any of claims 1 to 13, which hybridizes under low, preferably medium, and more preferably high, stringency conditions to (i) the nucleic acid sequence set forth in SEQ ID NO: 1 or SEQ ID NO: 48 or (ii) the respective complementary strand, or a subsequence thereof.

15. The nucleic acid sequence of claim 14, wherein low stringency conditions are defined by prehybridization and hybridization at 42°C in 5X SSPE, 0.3% SDS, 200 micro g/ml sheared and denatured salmon sperm DNA, and 25% formamide, and wash conditions are defined by 50°C for 30 minutes in 2X SSC, 0.2% SDS; medium stringency conditions are defined by prehybridization and hybridization at 42°C in 5x SSPE, 0.3% SDS, 200 microg/ml sheared and denatured salmon sperm DNA, and 35% formamide, and wash conditions are defined by 60°C for 30 minutes in 2X SSC, 0.2% SDS; and high stringency conditions are defined by prehybridization and hybridization at 42°C in 5x SSPE, 0.3% SDS, 200 microg/ml sheared and denatured salmon sperm DNA, and 50% formamide, and wash conditions are defined by 70°C for 30 minutes in 2X SSC, 0.2% SDS.

16. The nucleic acid sequence of any of claims 1 to 15, which comprises the nucleic acid sequence encoding a polypeptide, which has transcriptional activation activity contained in the plasmid pEES harboured in *Escherichia coli* DSM 12294 or DNA sequence shown in SEQ ID NO: 48 encoding polypeptide shown in SEQ ID NO: 49.

17. A nucleic acid construct comprising the nucleic acid sequence of any of claims 1 to 16 operably linked to one or more control sequences, which direct the production of the polypeptide in a suitable expression host.

18. An expression vector comprising the nucleic acid construct of claim 17, a promoter, and transcriptional and translational stop signals.

19. A host cell comprising the nucleic acid construct of claim 17 or the expression vector of claim 18.

20. An isolated polypeptide selected from the group consisting of:

(a) a polypeptide which is encoded in a nucleic acid sequence which hybridizes under low stringency conditions with (i) the nucleic acid sequence of SEQ ID NO: 1 or SEQ ID NO: 48; (ii) its complementary strand, or (iii) a subsequence of SEQ ID NO: 1 or SEQ ID NO: 48 which encodes a polypeptide fragment which has transcriptional activation activity, wherein the low stringency conditions are defined by prehybridization and hybridization at 42°C in 5X SSPE, 0.3% SDS, 200 micro g/ml sheared and denatured salmon sperm DNA, and 25% formamide, and wash conditions are defined at 50°C for 30 minutes in 2X SSC, 0.2% SDS;

(b) a polypeptide having an amino acid sequence which has at least 50% identity with the amino acid sequence of SEQ ID NO: 2 or SEQ ID NO: 49;

(c) an allelic variant of (a) or (b);

(d) a fragment of (a), (b), or (c), wherein the fragment has transcriptional activation activity; and

(e) a polypeptide comprising the amino acid sequence of SEQ ID NO: 3, or an allelic variant thereof.

21. The polypeptide of claim 20, comprising an amino acid sequence which has at least 50%, preferably at least 60%, preferably at least 70%, more preferably at least 80%, even more preferably at least 90%, more preferably at least 95%, even more preferred 97%, and most preferred 99% identity with the amino acid sequence of SEQ ID NO: 2 or SEQ ID NO: 49.

22. The polypeptide of claim 20 or 21, comprising the amino acid sequence of SEQ ID NO: 2 or SEQ ID NO: 49, or a fragment thereof, wherein the fragment retains transcriptional activation activity.

23. The polypeptide of any of claims 20 to 22 which is encoded in the nucleic acid sequence contained in plasmid pEES which is contained in *Escherichia coli* DSM 12294 or the DNA sequence shown in SEQ ID NO: 48.

24. The polypeptide of any of claims 20 to 23 which comprises the amino acid sequence of SEQ ID NO: 3.

25. A method for producing the polypeptide of any of claims 20 to 24 comprising (a) cultivating the host cell of claim 19 under conditions conducive for production of the polypeptide; and (b) recovering the polypeptide.

26. A fungal host cell useful for the production of a polypeptide, wherein the cell:

a) is a mutant of a parent fungal cell in which the parent cell comprises one or more DNA sequences encoding a protease, the transcription of which is activated by a transcriptional activator encoded by a nucleic acid sequence of any of claims 1 to 16; and

b) produces less of the transcriptional activator and the protease(s) than the parent cell when cultured under the same conditions.

27. The host cell of claim 26, wherein the reduced production of the transcriptional activator is obtained by modification or inactivation of a nucleic acid sequence present in the cell and necessary for expression of the transcriptional activator.

28. The host cell of claim 26 or 27, wherein the reduced production of the transcriptional activator is obtained by modification or inactivation of a control sequence required for the expression of the polypeptide.

29. The host cell of claim 28, wherein the control sequence is a promoter sequence, or a functional part thereof.

30. The host cell of any of claims 26 to 29, wherein the nucleic acid sequence to be modified or inactivated is the sequence defined in any of claims 1 to 16.

31. The host cell of any of claims 26 to 30, wherein the modification or inactivation is performed by specific or random mutagenesis, site-directed mutagensis, PCR generated mutagenesis, nucleotide insertion and/or substitution, gene interruption or gene replacement techniques, anti-sense techniques, or a combination thereof.

32. A fungal host cell useful for the production of a polypeptide, wherein the host cell is a mutant of a parent cell, in which the mutant:

a) produces more of a transcriptional activator encoded by a nucleic acid sequence of any of claims 1 to 16 than the parent cell when cultured under the same conditions, and

b) comprises a DNA sequence encoding the polypeptide, the transcription of which is activated by the transcriptional activator.

33. The host cell of claim 32, wherein the host cell produces more of the transcriptional activator than the parent cell by introducing into the parent cell one or more copies of: (i) a nucleic acid sequence of any of claims 1 to 16, (ii) the nucleic acid construct of claim 17, or (iii) the expression vector of claim 18, whereby the host cell produces more of the polypeptide than the parent cell when cultured under the same conditions.

34. The host cell of claim 32 or 33, wherein the nucleic acid acid sequence encoding the transcriptional activator is operably linked to a promoter, which is stronger than the corresponding promoter of the parent cell.

35. The host cell of claim 34, wherein the promoter mediates the expression of a gene encoding an extracellular protease, preferably *Aspergillus oryzae* alkaline protease, *A. oryzae* neutral

metalloprotease, *A. niger* aspergillopepsin protease, *Fusarium oxysporum* trypsin-like protease or *F. venenatum* trypsin.

36. A fungal host cell useful for the production of a polypeptide, wherein the cell is a mutant of a parent cell in which the mutant comprises:

a) a modification or inactivation of a transcriptional activator which is encoded in a native nucleic acid sequence of any of claims 1 to 16, or a regulatory sequence thereof, and

b) (i) an inducible promoter operably linked to a nucleic acid sequence of any of claims 1 to 16, and (ii) a promoter sequence to which a transcriptional activator encoded by the nucleic acid sequence of any of claims 1 to 16 can bind, operably linked to a nucleic acid sequence encoding the polypeptide, wherein (i) and (ii) can be introduced simultaneously or sequentially.

37. The host cell of claim 36 wherein the native nucleic acid sequence, or a regulatory sequence thereof, is modified or inactivated by specific or random mutagenesis, site-directed mutagensis, PCR generated mutagenesis, nucleotide insertion and/or substitution, gene interruption or gene replacement techniques, anti-sense techniques, or a combination thereof.

38. The host cell of claim 36 or 37, wherein the inducible promoter is selected from the group in which the induction is mediated by a carbon or nitrogen catabolite.

39. The host cell of any of claims 33 to 38, which further comprises a promoter sequence, wherein the promoter sequence can be activated by the transcriptional activator and is operably linked to the nucleic acid sequence encoding the polypeptide.

40. The host cell of any of claims 33 to 39, wherein the promoter sequence, or a functional part thereof, is from a protease gene.

41. The host cell of any of claims 33 to 40, wherein the protease gene is *Fusarium oxysporum* trypsin-like protease gene, *Aspegillus oryzae* alkaline protease gene, *Aspergillus niger pacA* gene, *Aspergillus oryzae* alkaline protease gene, *A. oryzae* neutral metalloprotease gene, *A. niger* aspergillopepsin protease gene, or *F. venenatum* trypsin gene.

42. The host cell of any of claims 26 to 41, wherein the host cell comprises at least one copy of a nucleic acid sequence encoding the polypeptide.

43. The host cell of any of claims 26 to 42, wherein the host cell produces less of a native protease or a combination of native proteases than the parent cell when cultured under identical conditions.

44. The host cell of any of claims 26 to 43, wherein the activity of the protease is assayed by the degradation of ^{3}H-labelled sperm whale myoglobin at pH 4.

45. A method of producing a polypeptide, comprising:

(a) cultivating the host cell of any of claims 26 to 44, wherein the host cell harbours a gene encoding the polypeptide, in a nutrient medium suitable for production of the polypeptide; and

(b) recovering the polypeptide from the nutrient medium of the mutant cell.

46. The method of claim 45, wherein the polypeptide is native to the parent cell.

47. The method of claim 45, wherein the polypeptide is heterologous to the parent cell.

48. The method of claim 45, wherein the polypeptide is an antibody or portions thereof, an antigen, a clotting factor, an enzyme, a hormone or a hormone variant, a receptor or portions thereof, a regulatory protein, a structural protein, a reporter, or a transport protein.

49. The method of claim 48, wherein the enzyme is an oxidoreductase, transferase, hydrolase, lyase, isomerase, or ligase.

50. The method of claim 49, wherein the enzyme is an aminopeptidase, amylase, carbohydrase, carboxypeptidase, catalase, cellulase, chitinase, cutinase, deoxyribonuclease, dextranase, esterase, alpha-galactosidase, beta-galactosidase, glucoamylase, alpha-glucosidase, beta-glucosidase, haloperoxidase, invertase, laccase, lipase, mannosidase, mutanase, oxidase, pectinolytic enzyme, peroxidase, phytase, polyphenoloxidase, proteolytic enzyme, ribonuclease, transglutaminase, or xylanase.

51. An isolated nucleic acid sequence, which comprises a sequence encoding a polypeptide that has transcriptional activation activity, wherein the sequence is:

(a) a nucleic acid sequence which hybridizes under high stringency conditions with (i) the nucleic acid sequence of SEQ ID NO: 48 or (ii) its complementary strand, wherein the high stringency conditions are defined by prehybridization and hybridization at 42°C in 5x SSPE, 0.3% SDS, 200 micrograms/ml sheared and denatured salmon sperm DNA, and 50% formamide, and washing at 65°C for 30 minutes in 2X SSC and 0.2% SDS; or

(b) a nucleic acid sequence that encodes a fragment of SEQ ID NO: 49, wherein the fragment has transcriptional activation activity.

52. The nucleic acid sequence of claim 51, which comprises a sequence encoding a polypeptide having an amino acid sequence that is at least 90% identical with the amino acid sequence of SEQ ID NO: 49.

53. The nucleic acid sequence of claim 52, which comprises a sequence encoding a polypeptide having an amino acid sequence that is at least 95% identical with the amino acid sequence of SEQ ID NO: 49.

54. The nucleic acid sequence of claim 53, which comprises a sequence encoding a polypeptide having an amino acid sequence that is at least 97% identical with the amino acid sequence of SEQ ID NO: 49.

55. The nucleic acid sequence of claim 54, which encodes a polypeptide having an amino acid sequence that is at least 99% identical with the amino acid sequence of SEQ ID NO: 49.

56. The nucleic acid sequence of claim 51, which encodes a polypeptide comprising the amino acid sequence of SEQ ID NO: 49.

57. The nucleic acid sequence of claim 56, which encodes a polypeptide consisting of the amino acid sequence of SEQ ID NO: 49.

58. The nucleic acid sequence of claim 51, wherein the nucleic acid sequence of nucleotides 977-3116 of SEQ ID NO: 48 or the cDNA thereof.

59. The nucleic acid sequence of claim 51, which hybridizes under said high stringency conditions with the nucleic acid sequence of SEQ ID NO: 48 or its complementary strand.

60. The nucleic acid sequence of claim 59, which encodes a polypeptide comprising the amino acid sequence of SEQ ID NO: 3.

61. The nucleic acid sequence of claim 59, which is obtained from an *Aspergillus* cell.

62. The nucleic acid sequence of claim 61, wherein the *Aspergillus* cell is an *Aspergillus oryzae* cell.

63. The nucleic acid sequence of claim 62, wherein the *Aspergillus* cell is *Aspergillus niger*, IFO 4177.

64. The nucleic acid sequence of claim 51, wherein the nucleic acid sequence is obtained from an *Aspergillus*, *Fusarium*, *Penicillium* or *Trichoderma* cell.

65. A nucleic acid construct comprising the nucleic acid sequence of claim 51 operably linked to one or more control sequences, which direct the production of the polypeptide in a suitable expression host.

66. An expression vector comprising the nucleic acid construct of claim 65, a promoter, and transcriptional and translational stop signals.

67. A host cell comprising the expression vector of claim 66.

68. A host cell useful for the production of a polypeptide, wherein the host cell is a mutant of a parent fungal cell and the host cell:

(a) comprises one or more DNA sequences encoding the polypeptide,

(b) comprises one or more DNA sequences encoding a protease or proteases, the transcription of which is or are activated by a transcriptional activator encoded by a nucleic acid sequence of claim 51; and

(c) produces less of the transcriptional activator and less of the protease or proteases compared to the parent fungal cell when cultured under the same conditions.

69. A method of producing a polypeptide, comprising:

(a) cultivating the host cell of claim 68, wherein the host cell harbors a gene encoding the desired polypeptide, in a nutrient medium suitable for production of the polypeptide; and

(b) recovering the polypeptide from the nutrient medium of the mutant cell.

70. The method of claim 69, wherein the polypeptide is native to the parent cell.

71. The method of claim 69, wherein the polypeptide is heterologous to the parent cell.

72. The method of claim 69, wherein the polypeptide is selected from the group consisting of an antibody or portions thereof, an antigen, a clotting factor, an enzyme, a hormone or a hormone variant, a receptor or portions thereof, a regulatory protein, a structural protein, a reporter, and a transport protein.

73. The method of claim 72, wherein the enzyme is selected from the group consisting of a hydrolase, isomerase, ligase, lyase, oxidoreductase, and transferase.

74. The method of claim 73, wherein the enzyme is selected from the group consisting of an aminopeptidase, amylase, carbohydrase, carboxypeptidase, catalase, cellulase, chitinase, cutinase, deoxyribonuclease, dextranase, esterase, alpha-galactosidase, beta-galactosidase, glucoamylase, alpha-glucosidase, beta-glucosidase, haloperoxidase, invertase, laccase, lipase, mannosidase, mutanase, oxidase, pectinolytic enzyme, peroxidase, phytase, polyphenoloxidase, proteolytic enzyme, ribonuclease, transglutaminase, and xylanase.

75. A host cell useful for the production of a protease, wherein the host cell is a mutant of a parent fungal cell and the host cell:

(a) comprises a DNA sequence encoding the protease, the transcription of which is activated by a transcriptional activator encoded by a nucleic acid sequence of claim 51, and

(b) produces more of the transcriptional activator than the parent fungal cell when cultured under the same conditions.

76. The host cell of claim 75, wherein the nucleic acid sequence encoding the transcriptional activator is operably linked to a promoter.

77. The host cell of claim 75, wherein the desired polypeptide is an extracellular protease.

78. A method of producing a protease, comprising:

(a) cultivating the host cell of claim 75 in a nutrient medium suitable for production of the protease; and

(b) recovering the protease from the nutrient medium of the mutant cell.

79. A host cell useful for the production of a desired polypeptide, wherein the cell is a mutant of a parent cell in which the mutant comprises:

(a) a modification or inactivation of a nucleic acid sequence of claim 92, so that the mutant produces less protease compared to the parent cell when cultured under the same conditions, and

(b) (i) an inducible promoter operably linked to a nucleic acid sequence of claim 51, and (ii) a promoter sequence that binds a transcriptional activator encoded by the nucleic acid sequence of claim 51, operably linked to a nucleic acid sequence encoding the desired polypeptide, wherein (i) and (ii) can be induced simultaneously or sequentially.

80. The host cell of claim 79, wherein the inducible promoter is mediated by a carbon or nitrogen catabolite.

81. The host cell of claim 79, wherein the promoter sequence that binds the transcriptional activator is from a protease gene.

82. A method of producing a desired polypeptide, comprising:

(a) cultivating the host cell of claim 79, wherein the host cell harbors a gene encoding the desired polypeptide, in a nutrient medium suitable for production of the desired polypeptide; and

(b) recovering the desired polypeptide from the nutrient medium of the mutant cell.